REMARKS

By the present amendment, claims 1, 10-11, and 16 have been amended. Support for the amendments are found in the original application, in particular on page 6, line 16 (claim 1), page 7, lines 27-28 (claim 10), original claims 12-13 (claim 11), and page 6, lines 19-28 (claim 16). Accordingly, claims 12-13 have been canceled. Further, new claim 17 has been added. Support for claim 17 is found in the original application, in particular on page 6, lines 24-27.

Claims 1-11, 14 and 16-17 are pending in the present application. The claims are directed to a method of sequence determination for nucleic acid. Claim 1 is the only independent claim.

As a preliminary, Applicants and Applicants' representative apologize for any awkwardness in the original specification and claims, which are translated from the Japanese language. It is submitted that, in spite of any colloquial imperfections that may be present due to the non-native English origin of the specification, these imperfections do not detract from the technical content of the application, which is set forth so as to be clearly and immediately understandable by a person of ordinary skill in the art focused on the teaching in the application.

Further, to illustrate how the inventive method makes it possible to obtain a matrix value of fluorochromes by using an actual sample instead of an exclusive reagent kit for calibration of the fluorochromes as in the conventional art, Applicants submit the attached charts that exemplify steps (1) to (6) of the claimed method with four fluorochrome detection parts as applied on an actual sample.

In step (1), starting portions of signals (peaks o, Δ) are extracted, so that clear peaks waveforms having excellent signal-to-noise ratios are generally obtained.

In step (2), peaks having irregular interval (Δ) are eliminated among the above extracted

peaks, so as to eliminate the overlapping peaks of bases.

In step (3), the remaining peaks (Δ) are classified in four groups according to signal strengths. The groups are:

G-group (G1-8): black > green > red > blue

A-group (A): green > red > blue > black

T-group (T1-3): red > blue > green > black

C-group (C): blue > red > green > black

In the definition of these groups, the terms "black", "green", "red" and "blue" mean the signal strengths of peak signals obtained by the fluorochromes detection parts for guanine, adenine, thymine, and cytosine, respectively. The peaks classified in other groups are eliminated as abnormal peaks since these peaks have low frequency of appearance. Also, when the signal strengths of fluorochromes of separated wavelengths are larger than those of fluorochromes of adjacent wavelengths, peaks thereof are eliminated as abnormality since overlapping of bases have occurred.

In step (4), the signal strength ratios are calculated. Various calculation methods such as mean values or central values are available. In this example, mean values are utilized. Thus, in the inventive method, the representative values of the signal strengths of "black", "green", "red", and "blue" by the inventive method are considered as the peak waveforms of peaks containing only one base, which can be used for calibration instead of the peak waveforms of peaks obtained utilizing an exclusive reagent kit.

In step (5), the corresponding bases are allocated to the classified four groups. Generally, the signal strength ratio is highest for the signal corresponding to the fluorochrome for the

corresponding base, so that the G-group is allocated to guanine, and the other A, T, and C groups are allocated to adenine, thymine, and cytosine, respectively. However, the signal strengths may be reversed due to sensitivity setting of detectors or the like, as illustrated on page 7 of the specification and Figure 5. In such a case, the allocation of bases can be carried out by utilizing the third largest signal, for example.

In step (6), the matrix value is obtained from signal strength ratios of peak wavelengths of the respective base groups. The matrix value is obtained by calculating the inverse matrix of the matrix of the signal strength ratios. This matrix illustrates the matrix M on page 2 of the specification, i.e., it represents the relationship between the emission strengths by the fluorochromes and the signal strengths detected by the detectors. Thus, a matrix M has been obtained based on an actual sample, instead of an exclusive reagent kit as in the conventional art.

Further, in the Advisory Action dated June 25, 2004, additional issues were listed regarding the claim language in the amendments of the response filed on June 10, 2004. These issues have been addressed by the present amendment as follows.

In claim 1, step (3), with respect to the expression "in response to the signal strengths for each of the remaining peaks", it was alleged that the description at page 6, line 16 only discloses "classify peaks in response to signal strengths". The phrase "for each of the remaining peaks" has now been deleted.

In claims 11-13, with respect to the expression "limited conditions", it was alleged that the description only discloses conditions limited as to the situations of page 8, lines 24-26. Claim 11 has been amended to incorporate the subject matter of claims 12-13, and claims 12-13 have been cancelled. It is submitted that the recitations of claims 12-13 now incorporated into claim 11

constitute proper illustrations of the "limited conditions" recited in claim 11, as suggested in the Advisory Action.

In claim 5, with respect to the expression "largest peak numbers", it was alleged that the description at page 6, lines 22-24 only discloses "larger peak numbers". The objection is respectfully traversed. It is submitted that a person of ordinary skill in the art would immediately understand that the expression "upper four groups having larger peak numbers" on page 6, lines 22-23, or "upper four groups having large peak numbers" in original claim 5, means "the four groups having the largest peak numbers". In particular, the following sentence indicates that the groups of abnormal peaks are eliminated based on their "small appearance frequency". Thus, the person of ordinary skill in the art would understand that the "upper four groups" are not random groups having large or larger peak numbers, but are the "upper" four groups, i.e., the four groups having the largest peak numbers.

In claims 6-7, with respect to the expression "central values", it is alleged that the explanation "array of values" is not recited in the claims. The objection is respectfully traversed. It is submitted that the terms "mean values" and "central values" are conventional in the statistical art, and that the explanation of "central" meaning the physical location of values in an array, i.e., a group of values was only submitted to illustrate the distinction between "mean values" and "central values".

In claim 10, with respect to the expression "optimized matrix", it was alleged that the description at page 7, lines 27-28 only discloses "optimum matrix value". The term "optimized" has been changed to "optimum" as suggested in the Advisory Action.

In claim 16, with respect to the expression "peaks having abnormal signal strengths", it is alleged that the description at page 6, lines 16-28 only discloses "abnormal peaks". Claim 16 has been amended to recite that "peaks classified in additional groups are eliminated as abnormal". Support for this recitation is found in the original application, in particular on page 6, lines 19-28. Specifically, it is submitted that the sentence at lines 19-22 explains that there may be more than four groups of peaks, i.e., there may be "additionally classified groups" (line 21). It is immediately understood from the following sentence (lines 22-24) that "such abnormal peaks" (lines 23-24) in these additional groups are not retained in the classification of the four groups, i.e., they are eliminated. Further, the next sentence (lines 24-27) describes the elimination of other peaks having "abnormality" and that sentence begins with "Also..." This grammatical construction confirms that the peaks in the additional groups, as well as the other abnormal peaks, are eliminated. Accordingly, new claim 17 has been added to define the abnormal peaks which are eliminated as described in the sentence on page 6, lines 24-27.

In view of the above, as well as the amendments and remarks set forth in the response filed on June 10, 2004, it is submitted that the rejections should be withdrawn.

In conclusion, the invention as presently claimed is patentable. It is believed that the claims are in allowable condition and a notice to that effect is earnestly requested.

In the event there is, in the Examiner's opinion, any outstanding issue and such issue may be resolved by means of a telephone interview, the Examiner is respectfully requested to contact the undersigned attorney at the telephone number listed below.

In the event this paper is not considered to be timely filed, the Applicants hereby petition for an appropriate extension of the response period. Please charge the fee for such extension and any other fees which may be required to our Deposit Account No. 50-2866.

Respectfully submitted,

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